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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,033	10/22/2001	Patrick C. Kung	YALE-025/02US 306577-2036	9303

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EXAMINER	
BORIN, MICHAEL L	

ART UNIT	PAPER NUMBER
1631	

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07/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/830,033	KUNG ET AL.	
	Examiner	Art Unit	
	Michael Borin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *83,84 and 87-89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *83,84,87-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Amendment filed 04/30/2009 is acknowledged. Claim 89 is added. Claims 83,84,87-89 are pending.

Claim Rejections - 35 USC § 103.

Claims 83,84,87-89 are rejected under 35 U.S.C. 103(a) as obvious over Khwaja et al (US Patent 6113907) in view of Lochardt (US patent 6040138) or Xiong et al. (Molecular Breeding 4: 129–136, 1998) and Wallace et al (Molecular Medicine Today. Volume 3, Issue 9, September 1997, pages 384-389), and further in view of Ray et al. (US 4,570,380)

The claims are directed to method for method for assessing the equivalency of a test batch of an herbal composition to a standardized batch by using genomic-based assay and comprising the steps of comparing gene expression detected by hybridizing test and standardized herbal compositions, comparing the gene expression, and assessing equivalency of expression in the test and standardized batches for the purposes of quality control.

Khwaja et al discloses a method for manufacturing pharmaceutical compositions from plant extracts wherein quality control is perform via standardization and control to provide reproducible material in the predictable and consistent treatment of patients (column 2, lines 39-51).

The method of Khwaja et al. comprises harvesting botanical material (whole or part), determining standardized bioactivity profile, comparing the calculated bioactivity of the botanical composition to a bioactivity fingerprint standard, and determine whether the botanical material is a pharmaceutical grade St. John's Wort (column 9, line 50 to column 2, line 7). The reference does not teach use of genomic based bioassays but teaches that use of bioassays is necessary for ensuring quality of a botanical product.

Complex plant materials and extracts exist which have potent, but relatively unpredictable, medicinal properties. These materials are, for the most part, useless in a clinical setting because of the inherent risks involved with treating patients with poorly characterized materials which have no established batch consistency and which may differ widely in composition. Accordingly, there is a need to provide methods for standardizing such complex botanical materials

The use of gene arrays for content control is well known in the art. See, for example Lochardt (US patent 6040138) describing use of gene arrays for monitoring the expression levels of a multiplicity of pre-selected genes in the presence of large abundance of non-target nucleic acids. See abstract and col. 2. The gene array method of Lochardt is useful in particular for identification of differential gene expression between two samples. See col. 10, line 23. Alternatively see Xiong et al. teaching differential gene expression profile of the whole batch of plant extract via a genomic-based bioassay. See Abstract.

Also see review of Wallace et al emphasizing that DNA chips is a major advance in testing complex mixtures which provide much faster and more reliable assay. See Abstract and throughout the reference.

Further, one skilled in the botanical art at the time the invention was made was fully aware of gene expression in plants, importance of understanding of gene

expression for quality control - See Ray et al, (Abstract (last two lines) and claims 1-22, for example) – as well of use of differential gene expression profiles of the whole batch of plant extract via a genomic-based bioassay - see Xiong et al.

In *KSR Int 'l v. Teleflex*, the Supreme Court, in rejecting the rigid application of the teaching, suggestion, and motivation test by the Federal Circuit, indicated that

> The principles underlying [earlier] cases are instructive when the question is whether a patent claiming the combination of elements of prior art is obvious. When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability.

KSR Int'l v. Teleflex Inc., 127 S. Ct. 1727, 1740 (2007).

Applying the KSR standard of obviousness to the references discussed above, Examiner concludes that using the known technique of gene array analysis of gene expression instead of bioassay in the method of Khwaja et al would have been obvious to one of ordinary skill. The nature of the problem to be solved – comparison between herbal compositions for the purpose of quality control may lead inventors to look at references relating to new and improved methods of assaying the content of herbal compositions. Therefore, it would have been obvious to use the more advanced method of gene expression analysis described, for example in Lochardt , Xiong or Wallace. As one skilled in the botanical art was aware of importance of understanding of gene expression for quality control, using the known technique gene expression analysis to

provide the desired information for the quality control would have been obvious to one of ordinary skill.

In addition it will be *prima facie* obvious to one skilled in the art at the time the invention was made to be motivated to use genomic-based assays, such as described in Lochardt or Xiong or Ray or Wallace, for example, in the method of Khwaja et al to provide control of the content of herbal preparations samples in the method of Khwaja. One of ordinary skill in the art would not be confined by the particular assays taught in the method of Khwaja and will have reasonable expectation of success that genomic-based assays will be equally effective.

With regard to newly added claim 89, Khwaja teach that bioassay can be based on animal cell or tissue activity. See col. 22, lines 56-61, col. 23, lines 24-27.

Response to arguments

Applicant's concerns are considered but are not deemed persuasive. The majority of arguments have been already addressed in the preceding Office action.

In this response Applicants have traversed the primary and the secondary references pointing to the differences between the claims and the disclosure in each reference. Applicant is respectfully reminded that the rejection is under 35 USC103 and that unobviousness cannot be established by attacking the references individually when the rejection is based on the combination of the references. It has been well established that the test for combining references is not what individual references

themselves suggest but what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. *In re McLaughlin,* 170 USPQ 209 (CCPA 1970).

The rejection is maintained and extended to new claim 89.

Prior art made of record

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Hylands et al (6806090) teaches method for quality control and standardization of medicinal plant products comprising preparing solutions or extracts of standard and test samples of whole plant product and comparing them using one or more biological profiling techniques, such as proteomic analysis (see Example 6).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571)272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Borin/
Primary Examiner, Art Unit 1631

mlb